GenCore version 5.1.6

OM protein - protein search, using sw model

Run on: May 23, 2005, 15:30:19 ; Search time 69 Seconds
(without alignments)
263.445 Million cell updates/sec

Title: US-09-107-979-4
Perfect score: 277
Sequence: 1 HFKPCRDKDLAYCLNDGECF.....SHKHCRCKEGYQGVRCDQFL 47

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 2105692 seqs, 386760381 residues

Total number of hits satisfying chosen parameters: 2105692

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : A_Geneseq_16Dec04:*
1: geneseqp1980s:*
2: geneseqp1990s:*
3: geneseqp2000s:*
4: geneseqp2001s:*
5: geneseqp2002s:*
6: geneseqp2003as:*
7: geneseqp2003bs:*
8: geneseqp2004s:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	277	100.0	47	2	AAW97622	Aaw97622 Human neu
2	277	100.0	48	5	AAG66046	Aag66046 Mouse NRG
3	277	100.0	52	6	AAE36807	Aae36807 Human neu
4	277	100.0	157	2	AAY05451	Aay05451 Human her
5	277	100.0	157	8	ADN48870	Adn48870 Human her
6	277	100.0	360	2	AAW97621	Aaw97621 Human neu
7	277	100.0	362	2	AAW97620	Aaw97620 Mouse neu
8	277	100.0	502	5	ABB08776	Abb08776 Human neu
9	277	100.0	696	2	AAW97619	Aaw97619 Human neu
10	277	100.0	696	5	ABG32080	Abg32080 Novel hum
11	277	100.0	713	2	AAW97617	Aaw97617 Mouse neu
12	277	100.0	713	5	ABG32061	Abg32061 Mouse nov
13	277	100.0	720	2	AAW97618	Aaw97618 Human neu
14	277	100.0	720	2	AAY05452	Aay05452 Human her
15	277	100.0	720	5	ABG32065	Abg32065 Human nov
16	277	100.0	720	8	ADN48890	Adn48890 Human her
17	116.5	42.1	52	2	AAW05182	Aaw05182 Neu diffe
18	116.5	42.1	52	3	AAY69983	Aay69983 NDF/hereg
19	116.5	42.1	52	3	AAB12602	Aab12602 Human NDF
20	113.5	41.0	52	2	AAW05184	Aaw05184 Neu diffe
21	113.5	41.0	53	6	AAE36803	Aae36803 Human neu
22	113.5	41.0	53	8	ADN48885	Adn48885 Human her
23	113.5	41.0	63	2	AAR55659	Aar55659 EGFL2. 3/
24	113.5	41.0	63	2	AAR46918	Aar46918 EGFL2. 3/
25	113.5	41.0	63	2	AAR67250	Aar67250 Human epi
26	113.5	41.0	63	2	AAR96076	Aar96076 Epidermal
27	113.5	41.0	63	2	AAW09363	Aaw09363 EGFL2. 8/
28	113.5	41.0	63	2	AAR87461	Aar87461 Epidermal
29	113.5	41.0	66	3	AAB36702	Aab36702 EGF-like
30	113.5	41.0	83	2	AAR55663	Aar55663 EGFL6. 3/
31	113.5	41.0	83	2	AAR46922	Aar46922 EGFL6. 3/
32	113.5	41.0	83	2	AAR67254	Aar67254 Human epi
33	113.5	41.0	83	2	AAR96080	Aar96080 Epidermal
34	113.5	41.0	83	2	AAW09367	Aaw09367 EGFL6. 8/
35	113.5	41.0	83	2	AAR87465	Aar87465 Epidermal
36	113.5	41.0	88	2	AAR55662	Aar55662 EGFL5. 3/
37	113.5	41.0	88	2	AAR46921	Aar46921 EGFL5. 3/
38	113.5	41.0	88	2	AAR67253	Aar67253 Human epi
39	113.5	41.0	88	2	AAR96079	Aar96079 Epidermal
40	113.5	41.0	88	2	AAW09366	Aaw09366 EGFL5. 8/
41	113.5	41.0	88	2	AAR87464	Aar87464 Epidermal
42	113.5	41.0	99	5	ABJ00043	Abj00043 Human neu
43	113.5	41.0	99	5	ABJ00081	Abj00081 Human neu
44	113.5	41.0	99	8	ADH77520	Adh77520 Human neu
45	113.5	41.0	101	4	AAG67933	Aag67933 Human NRG

ALIGNMENTS

RESULT 1
AAW97622
ID AAW97622 standard; protein; 47 AA.
XX
AC AAW97622;
XX
DT 10-MAY-1999 (first entry)
XX
DE Human neuregulin related ligand NRG3 EGF-like domain.
XX
KW Neuregulin related ligand; NRG3; hNRG3B1; human; ErbB4 receptor;
KW signal transduction; nervous system disorder; neurodegeneration;
KW neuropathy; therapy; diagnosis; epidermal growth factor; EGF;
KW immunoadhesin.
XX
OS Homo sapiens.
XX
PN WO9902681-A1.
XX
PD 21-JAN-1999.
XX
PF 30-JUN-1998; 98WO-US013411.
XX
PR 09-JUL-1997; 97US-0052019P.
PR 24-JUL-1997; 97US-00899437.
XX
PA (GETH) GENENTECH INC.
XX
PI Godowski PJ, Mark MR, Zhang D;
XX
DR WPI; 1999-120882/10.
XX
PT New isolated neuregulin related ligand-3 - used to develop products for
PT treating nervous system disorders, e.g. stroke, ischaemia, infection,
PT malignancy, Alzheimer's disease or Down's syndrome.
XX
PS Claim 30; Page 64; 101pp; English.
XX
CC This is the epidermal growth factor (EGF)-like domain of human neuregulin
CC related ligand NRG3 (see also AAW97618), a novel member of the EGF-like
CC family of protein ligands that binds to the ErbB4 receptor and activates
CC ErbB4 receptor tyrosine phosphorylation. The EGF-1 like domain of NRG3 is
CC distinct from the EGF-like domains of NRG1 and NRH2. The invention
CC provides human and murine polypeptides (see also AAW97617) that have at
CC least 75% homology to the NRG3 EGF-like domain, as well as expression
CC vectors, host cells and methods for the recombinant production of novel
CC NRG3s. The NRG3 polypeptides and polynucleotides and can be used to
CC enhance the survival, proliferation or differentiation of cells having

CC the ErbB4 receptor in vivo and in vitro. They can be used to prevent or
CC treat damage to a nerve or damage to other NRG3-expressing or NRG3-
CC responsive cells, e.g. brain, heart, or kidney cells. In particular, they
CC can be used to treat diseases which involve neural cell growth such as
CC demyelination, or damage or loss of glial cells (e.g. multiple
CC sclerosis). They can be used to treat patients whose nervous system has
CC been damaged by e.g. trauma, surgery, stroke, ischaemia, infection,
CC metabolic disease, nutritional deficiency, malignancy, or toxic agents.
CC NRG3 can also be used to treat motor neuron disorders such as amyotrophic
CC lateral sclerosis (Lou Gehrig's disease), Bell's palsy, conditions
CC involving spinal muscular atrophy or paralysis, neurodegenerative
CC disorders such as Alzheimer's disease, Parkinson's disease, epilepsy,
CC multiple sclerosis, Huntington's chorea, Down's syndrome, nerve deafness,
CC and Meniere's disease. They can also be used to treat neuropathies
CC associated with systemic disease including post-polio syndrome,
CC hereditary neuropathies including Charcot-Marie-Tooth disease, Refsum's
CC disease, abetalipoproteinemia, Tangier disease, Krabbe's disease,
CC metachromatic leukodystrophy, Fabry's disease and Dejerine-Sottas
CC syndrome, to treat disease of skeletal muscle of smooth muscle, such as
CC muscular dystrophy or diseases caused by skeletal or smooth muscle
CC wasting. The products can also be used for detection, diagnosis, for the
CC production of transgenic or knockout animals or for drug screening. A
CC claimed immunoadhesin comprises the human NRG3 EGF-like domain fused to
CC an immunoglobulin sequence
XX
SQ Sequence 47 AA;

Query Match 100.0%; Score 277; DB 2; Length 47;
Best Local Similarity 100.0%; Pred. No. 7.5e-21;
Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 47
||||||||||||||||||||||||||||||||||||||||||||||||
Db 1 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 47

RESULT 2
AAG66046
ID AAG66046 standard; peptide; 48 AA.
XX
AC AAG66046;
XX
DT 27-FEB-2002 (first entry)
XX
DE Mouse NRG-3 EGF-like motif sequence.
XX
KW ErbB-4; neuregulin-4; NRG-4; pro-NRG-4; neuroprotective; vulnerary;
KW cerebroprotective; vasotropic; antiparkinsonian; anticonvulsant;
KW cytostatic; nootropic; EGF; NRG-3.
XX
OS Mus musculus.
XX
PN WO200181540-A2.
XX
PD 01-NOV-2001.
XX
PF 20-APR-2001; 2001WO-IL000371.
XX
PR 21-APR-2000; 2000US-00553769.
XX
PA (YEDA) YEDA RES & DEV CO LTD.
XX
PI Harari D, Yarden Y;
XX
DR WPI; 2002-041398/05.
XX
PT Novel ErbB-4 ligand, referred as neuregulin (NRG)-4 and polynucleotide
PT sequences encoding NRG-4, useful for upregulating or downregulating ErbB-
PT 4 receptor activity to treat Alzheimer's disease, stroke, gastric cancer.
XX
PS Disclosure; Fig 1c; 153pp; English.
XX
CC The invention relates to a novel ErbB-4 ligand, neuregulin-4 (NRG-4). NRG
CC -4 binds to mammalian ErbB-4 receptor and can be expressed by standard
CC recombinant methodology. Pharmaceutical compositions comprising NRG-4 are
CC useful for regulating an endogenous protein affecting ErbB-4 receptor
CC activity in vivo. They are also useful for treating or preventing a
CC disease condition or syndrome associated with disregulation of an
CC endogenous protein affecting ErbB-4 receptor activity, e.g., amyotrophic
CC lateral sclerosis (Lou Gehrig's disease), Bell's palsy, spinal muscular
CC atrophy, brain trauma, stroke, ischemia, Alzheimer's disease, Parkinson's
CC disease, epilepsy, multiple sclerosis, Huntington's chorea, Down's
CC syndrome, nerve deafness, neuropathy, muscular dystrophy, extramammary
CC Paget's disease, gastric, pancreatic, prostate, breast and ovarian
CC cancer, cervical carcinoma, endometrial adenocarcinoma, pancreatic D
CC cells-somatostatinoma and Zollinger-Ellison syndrome. The agent comprised
CC in the pharmaceutical composition includes a polypeptide (e.g., a soluble
CC ligand binding domain of ErbB-4 i.e., IgB4; or a monoclonal, polyclonal,
CC humanized, single chain antibody or an immunoreactive derivative of an
CC antibody) capable of binding the endogenous protein affecting ErbB-4
CC receptor activity. Traceable synthetic/recombinant NRG-4-tagged molecules
CC can serve as a diagnostic tool in which cells binding NRG-4 can be
CC measured. Sequences AAG66044-53 represent the EGF-like motifs of various
CC growth factors
XX
SQ Sequence 48 AA;

Query Match 100.0%; Score 277; DB 5; Length 48;
Best Local Similarity 100.0%; Pred. No. 7.6e-21;
Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 47
||||||||||||||||||||||||||||||||||||||||||||||||
Db 2 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 48

RESULT 3
AAE36807
ID AAE36807 standard; protein; 52 AA.
XX
AC AAE36807;
XX
DT 07-AUG-2003 (first entry)
XX
DE Human neuregulin 3 EGF-like domain.
XX
KW Epidermal growth factor receptor; EGFR; therapy; psoriasis; carcinoma;
KW cancer; rhabdomyosarcoma; mesothelioma; melanoma; glioblastoma; human;
KW receptor; EGF; neuregulin 3.
XX
OS Homo sapiens.
XX
PN WO2003014159-A1.
XX
PD 20-FEB-2003.
XX
PF 05-AUG-2002; 2002WO-AU001042.
XX
PR 03-AUG-2001; 2001AU-00006827.
PR 03-AUG-2001; 2001AU-00006828.
PR 01-NOV-2001; 2001US-0335393P.
PR 01-NOV-2001; 2001US-0336560P.
PR 31-MAY-2002; 2002AU-00002731.
PR 11-JUN-2002; 2002US-0388171P.
XX
PA (CSIR) COMMONWEALTH SCI & IND RES ORG.
PA (BIOM-) BIOMOLECULAR RES INST LTD.
PA (HALL-) HALL INST MEDICAL RES WALTER & ELIZA.
PA (LUDW-) LUDWIG INST CANCER RES.
XX
PI Adams TE, Burgess AW, Elleman TC, Garrett TPJ, Jorissen RN;
PI Lou M, Lovrecz GO, Mckern NM, Nice EC, Ward CW;
XX
DR WPI; 2003-268181/26.
XX
PT Selecting or designing compounds that interact with or inhibit formation

PT of active dimers of the EGF receptor family, and useful for the
PT prevention and treatment of disorders, such as psoriasis and cancer of
PT the breast, brain or colon.
XX
PS Disclosure; Fig 2; 354pp; English.
XX
CC The invention relates to a method of selecting or designing a compound
CC that interacts with or inhibits the formation of active dimers of a
CC receptor of the epidermal growth factor receptor (EGFR) family. The
CC methods and compositions of the invention are useful for the prevention
CC and treatment of disorders associated with signalling by a molecule of
CC the EGFR family such as psoriasis and cancer of the pancreas, breast,
CC brain, colon, prostate, ovary, cervix, lung, head and neck, melanoma,
CC rhabdomyosarcoma, mesothelioma, squamous carcinomas of the skin and
CC glioblastomas. The present sequence is epidermal growth factor (EGF) like
CC domain of human neuregulin 3 protein. This sequence is used to illustrate
CC the method of the invention
XX
SQ Sequence 52 AA;

Query Match 100.0%; Score 277; DB 6; Length 52;
Best Local Similarity 100.0%; Pred. No. 8.2e-21;
Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 47
||||||||||||||||||||||||||||||||||||||||||||||||
Db 2 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 48

RESULT 4
AAY05451
ID AAY05451 standard; protein; 157 AA.
XX
AC AAY05451;
XX
DT 06-JUL-1999 (first entry)
XX
DE Human heregulin-like factor sequence.
XX
KW Human heregulin-like factor; HLF; cell growth regulator; diagnosis;
KW neural system disorder; cancer.
XX
OS Homo sapiens.
XX
PN WO9857989-A1.
XX
PD 23-DEC-1998.
XX
PF 16-JUN-1998; 98WO-US012403.
XX
PR 17-JUN-1997; 97US-0049942P.
XX
PA (HUMA-) HUMAN GENOME SCI INC.
PA (GEOU) UNIV GEORGETOWN.
XX
PI Young P, Ruben SM, King CR, Hijazi MM;
XX
DR WPI; 1999-095327/08.
DR N-PSDB; AAX36423.
XX
PT New isolated heregulin-like factor - used to develop products for the
PT diagnosis and treatment of disorders involving regulation of cell growth,
PT particularly cancers.
XX
PS Claim 17; Page 86-87; 118pp; English.
XX
CC This sequence is the human heregulin-like factor (HLF) of the invention.
CC The HLF is involved in the regulation of cell growth. Detection of
CC different levels of expression of the HLF gene can be used for the
CC diagnosis of disorders, e.g. in the neural system. In particular,
CC detection of different levels of HLF gene expression in cells or body
CC fluid of an individual can be used for diagnosing cancer. The products
CC can also be used in the treatment of disorders involving abnormal levels
CC of HLF activity
XX
SQ Sequence 157 AA;

Query Match 100.0%; Score 277; DB 2; Length 157;
Best Local Similarity 100.0%; Pred. No. 2.3e-20;
Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 47
||||||||||||||||||||||||||||||||||||||||||||||||
Db 31 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 77

RESULT 5
ADN48870
ID ADN48870 standard; protein; 157 AA.
XX
AC ADN48870;
XX
DT 15-JUL-2004 (first entry)
XX
DE Human heregulin-like factor (HLF) protein.
XX
KW HLF; heregulin-like factor; diagnosis; cancer; gene therapy; human.
XX
OS Homo sapiens.
XX
FH Key Location/Qualifiers
FT Domain 26. .93
FT /note = EGF domain
XX
PN US6727077-B1.
XX
PD 27-APR-2004.
XX
PF 16-JUN-1998; 98US-00097681.
XX
PR 17-JUN-1997; 97US-0049492P.
XX
PA (HUMA-) HUMAN GENOME SCI INC.
PA (GEOU) UNIV GEORGETOWN MEDICAL CENT.
XX
PI Young PE, King CR, Hijazi M, Ruben SM;
XX
DR WPI; 2004-338520/31.
DR N-PSDB; ADN48869.
XX
PT New heregulin-like factor (HLF) nucleic acid or polypeptide, useful for
PT preparing a composition for diagnosing or treating cancer.
XX
PS Claim 1; SEQ ID NO 2; 48pp; English.
XX
CC The present invention relates to novel heregulin-like factor (HLF)
CC polypeptides and the encoding polynucleotides. The invention is useful
CC for preparing a composition for diagnosing and treating cancer. The
CC invention is also useful in gene therapy. The present sequence is human
CC heregulin-like factor (HLF) protein.
XX
SQ Sequence 157 AA;

Query Match 100.0%; Score 277; DB 8; Length 157;
Best Local Similarity 100.0%; Pred. No. 2.3e-20;
Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 47
||||||||||||||||||||||||||||||||||||||||||||||||
Db 31 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 77

RESULT 6
AAW97621
ID AAW97621 standard; protein; 360 AA.
XX

AC AAW97621;
XX
DT 10-MAY-1999 (first entry)
XX
DE Human neuregulin related ligand NRG3 extracellular domain.
XX
KW Neuregulin related ligand; NRG3; hNRG3B1; human; ErbB4 receptor;
KW signal transduction; nervous system disorder; neurodegeneration;
KW neuropathy; therapy; diagnosis.
XX
OS Homo sapiens.
XX
PN WO9902681-A1.
XX
PD 21-JAN-1999.
XX
PF 30-JUN-1998; 98WO-US013411.
XX
PR 09-JUL-1997; 97US-0052019P.
PR 24-JUL-1997; 97US-00899437.
XX
PA (GETH) GENENTECH INC.
XX
PI Godowski PJ, Mark MR, Zhang D;
XX
DR WPI; 1999-120882/10.
XX
PT New isolated neuregulin related ligand-3 - used to develop products for
PT treating nervous system disorders, e.g. stroke, ischaemia, infection,
PT malignancy, Alzheimer's disease or Down's syndrome.
XX
PS Claim 5(a); Page 69-70; 101pp; English.
XX
CC This is the extracellular domain (ECD, aa1-360 of human neuregulin
CC related ligand NRG3 (see also AAW97618), a novel member of the epidermal
CC growth factor (EGF)-like family of protein ligands. NRG3 binds to the
CC ErbB4 receptor, but not to the ErbB2 or ErbB3 receptor, activates ErbB4
CC receptor tyrosine phosphorylation. The invention provides human and
CC murine polypeptides (see also AAW97617) that have at least 75% homology
CC to the NRG3 ECD, as well as expression vectors, host cells and methods
CC for the recombinant production of novel NRG3s. The NRG3 polypeptides and
CC polynucleotides and can be used to enhance the survival, proliferation or
CC differentiation of cells having the ErbB4 receptor in vivo and in vitro.
CC They can be used to prevent or treat damage to a nerve or damage to other
CC NRG3-expressing or NRG3-responsive cells, e.g. brain, heart, or kidney
CC cells. In particular, they can be used to treat diseases which involve
CC neural cell growth such as demyelination, or damage or loss of glial
CC cells (e.g. multiple sclerosis). They can be used to treat patients whose
CC nervous system has been damaged by e.g. trauma, surgery, stroke,
CC ischaemia, infection, metabolic disease, nutritional deficiency,
CC malignancy, or toxic agents. NRG3 can also be used to treat motor neuron
CC disorders such as amyotrophic lateral sclerosis (Lou Gehrig's disease),
CC Bell's palsy, conditions involving spinal muscular atrophy or paralysis,
CC neurodegenerative disorders such as Alzheimer's disease, Parkinson's
CC disease, epilepsy, multiple sclerosis, Huntington's chorea, Down's
CC syndrome, nerve deafness, and Meniere's disease. They can also be used to
CC treat neuropathies associated with systemic disease including post-polio
CC syndrome, hereditary neuropathies including Charcot-Marie-Tooth disease,
CC Refsum's disease, abetalipoproteinemia, Tangier disease, Krabbe's
CC disease, metachromatic leukodystrophy, Fabry's disease and Dejerine-
CC Sottas syndrome, to treat disease of skeletal muscle of smooth muscle,
CC such as muscular dystrophy or diseases caused by skeletal or smooth
CC muscle wasting. The products can also be used for detection, diagnosis,
CC for the production of transgenic or knockout animals or for drug
CC screening
XX
SQ Sequence 360 AA;

Query Match 100.0%; Score 277; DB 2; Length 360;
Best Local Similarity 100.0%; Pred. No. 4.8e-20;
Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 47
||||||||||||||||||||||||||||||||||||||||||||||||
Db 286 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 332

RESULT 7
AAW97620
ID AAW97620 standard; protein; 362 AA.
XX
AC AAW97620;
XX
DT 10-MAY-1999 (first entry)
XX
DE Mouse neuregulin related ligand NRG3 extracellular domain.
XX
KW Neuregulin related ligand; NRG3; mouse; ErbB4 receptor;
KW signal transduction; nervous system disorder; neurodegeneration;
KW neuropathy; therapy; diagnosis.
XX
OS Mus sp.
XX
PN WO9902681-A1.
XX
PD 21-JAN-1999.
XX
PF 30-JUN-1998; 98WO-US013411.
XX
PR 09-JUL-1997; 97US-0052019P.
PR 24-JUL-1997; 97US-00899437.
XX
PA (GETH) GENENTECH INC.
XX
PI Godowski PJ, Mark MR, Zhang D;
XX
DR WPI; 1999-120882/10.
XX
PT New isolated neuregulin related ligand-3 - used to develop products for
PT treating nervous system disorders, e.g. stroke, ischaemia, infection,
PT malignancy, Alzheimer's disease or Down's syndrome.
XX
PS Claim 5(a); Page 62-63; 101pp; English.
XX
CC This is the extracellular domain (ECD, aa1-362) of murine neuregulin
CC related ligand NRG3 (see also AAW97617), a novel member of the epidermal
CC growth factor (EGF)-like family of protein ligands. NRG3 binds to the
CC ErbB4 receptor, but not to the ErbB2 or ErbB3 receptor, activates ErbB4
CC receptor tyrosine phosphorylation. The invention provides human and
CC murine polypeptides (see also AAW97618) that have at least 75% homology
CC to the NRG3 ECD, as well as expression vectors, host cells and methods
CC for the recombinant production of novel NRG3s. The NRG3 polypeptides and
CC polynucleotides and can be used to enhance the survival, proliferation or
CC differentiation of cells having the ErbB4 receptor in vivo and in vitro.
CC They can be used to prevent or treat damage to a nerve or damage to other
CC NRG3-expressing or NRG3-responsive cells, e.g. brain, heart, or kidney
CC cells. In particular, they can be used to treat diseases which involve
CC neural cell growth such as demyelination, or damage or loss of glial
CC cells (e.g. multiple sclerosis). They can be used to treat patients whose
CC nervous system has been damaged by e.g. trauma, surgery, stroke,
CC ischaemia, infection, metabolic disease, nutritional deficiency,
CC malignancy, or toxic agents. NRG3 can also be used to treat motor neuron
CC disorders such as amyotrophic lateral sclerosis (Lou Gehrig's disease),
CC Bell's palsy, conditions involving spinal muscular atrophy or paralysis,
CC neurodegenerative disorders such as Alzheimer's disease, Parkinson's
CC disease, epilepsy, multiple sclerosis, Huntington's chorea, Down's
CC syndrome, nerve deafness, and Meniere's disease. They can also be used to
CC treat neuropathies associated with systemic disease including post-polio
CC syndrome, hereditary neuropathies including Charcot-Marie-Tooth disease,
CC Refsum's disease, abetalipoproteinemia, Tangier disease, Krabbe's
CC disease, metachromatic leukodystrophy, Fabry's disease and Dejerine-
CC Sottas syndrome, to treat disease of skeletal muscle of smooth muscle,
CC such as muscular dystrophy or diseases caused by skeletal or smooth
CC muscle wasting. The products can also be used for detection, diagnosis,
CC for the production of transgenic or knockout animals or for drug
CC screening

```
XX
SQ   Sequence 362 AA;

  Query Match            100.0%;  Score 277;  DB 2;  Length 362;
  Best Local Similarity  100.0%;  Pred. No. 4.9e-20;
  Matches   47;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 47
              |||||||||||||||||||||||||||||||||||||||||||||||
Db        288 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 334


RESULT 8
ABB08776
ID   ABB08776 standard; protein; 502 AA.
XX
AC   ABB08776;
XX
DT   16-MAY-2002  (first entry)
XX
DE   Human neuregulin 55 SEQ ID NO 2.
XX
KW   Human; neuregulin 55; nervous system; development; neuropsychopathy;
KW   tumour; inflammation; immunological disease.
XX
OS   Homo sapiens.
XX
PN   CN1324826-A.
XX
PD   05-DEC-2001.
XX
PF   19-MAY-2000; 2000CN-00115761.
XX
PR   19-MAY-2000; 2000CN-00115761.
XX
PA   (BODE-) BODE GENE DEV CO LTD SHANGHAI.
XX
PI   Mao Y,  Xie Y;
XX
DR   WPI; 2002-217507/28.
DR   N-PSDB; ABL41244.
XX
PT   New polypeptide human neuregulin 55 and polynucleotides for encoding
PT   same.
XX
PS   Claim 1; Page 27-28 (Disclosure); 35pp; Chinese.
XX
CC   The invention relates to human neuregulin 55, polynucleotide for coding
CC   this polypeptide and a method for producing this polypeptide by using DNA
CC   recombination technique. The invention also discloses the method for
CC   curing several diseases, such as nervous system developmental diseases,
CC   neuropsychopathy, other nervous system diseases, development disturbance,
CC   tumours, inflammations and immunological disease by using said
CC   polypeptide. The invention also discloses an antagonist for resisting
CC   said polypeptide and its therapeutic action and also discloses the
CC   application of polynucleotide to coding this novel human neuregulin 55.
CC   The present sequence is that of human neuregulin 55
XX
SQ   Sequence 502 AA;

  Query Match            100.0%;  Score 277;  DB 5;  Length 502;
  Best Local Similarity  100.0%;  Pred. No. 6.6e-20;
  Matches   47;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 47
              |||||||||||||||||||||||||||||||||||||||||||||||
Db         92 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 138


RESULT 9
AAW97619
ID   AAW97619 standard; protein; 696 AA.
XX
AC   AAW97619;
XX
DT   10-MAY-1999  (first entry)
XX
DE   Human neuregulin related ligand NRG3 (splice variant).
XX
KW   Neuregulin related ligand; NRG3; hNRG3B1; human; ErbB4 receptor;
KW   signal transduction; nervous system disorder; neurodegeneration;
KW   neuropathy; therapy; diagnosis; splice variant.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Domain          1. .360
FT                   /note= "extracellular domain, specifically claimed in
FT                   Claim 5(a)"
FT   Region          66. .91
FT                   /note= "hydrophobic region"
FT   Region          101. .284
FT                   /note= "mucin-like Ser/Thr-rich region, contains sites
FT                   for O-linked glycosylation"
FT   Domain          285. .354
FT                   /note= "EGF-like domain"
FT   Domain          356. .394
FT                   /note= "transmembrane domain"
XX
PN   WO9902681-A1.
XX
PD   21-JAN-1999.
XX
PF   30-JUN-1998;   98WO-US013411.
XX
PR   09-JUL-1997;   97US-0052019P.
PR   24-JUL-1997;   97US-00899437.
XX
PA   (GETH ) GENENTECH INC.
XX
PI   Godowski PJ,  Mark MR,  Zhang D;
XX
DR   WPI; 1999-120882/10.
DR   N-PSDB; AAX06989.
XX
PT   New isolated neuregulin related ligand-3 - used to develop products for
PT   treating nervous system disorders, e.g. stroke, ischaemia, infection,
PT   malignancy, Alzheimer's disease or Down's syndrome.
XX
PS   Example 1; Page 78-81; 101pp; English.
XX
CC   This is the amino acid sequence of splice variant hNGR3B2 of human
CC   neuregulin related ligand NRG3, a novel member of the epidermal growth
CC   factor (EGF)-like family of protein ligands that binds to the ErbB4
CC   receptor, but not to the ErbB2 or ErbB3 receptor, and which activates
CC   ErbB4 receptor tyrosine phosphorylation. The sequence was deduced from
CC   the nucleotide sequence of a cDNA clone (see AAX06989) from a foetal
CC   brain library. hNGR3B2 lacks amino acids 529-552 of hNGR3B1 (see
CC   AAW97618) but retains the EGF- like domain and is expected to exhibit
CC   biological activity. The invention provides human and murine NRG3
CC   polypeptides (see AAW97617), expression vectors, host cells and methods
CC   for the recombinant production of NRG3s. The NRG3 polypeptides and
CC   polynucleotides and can be used to enhance the survival, proliferation or
CC   differentiation of cells having the ErbB4 receptor in vivo and in vitro.
CC   They can be used to prevent or treat damage to a nerve or damage to other
CC   NRG3-expressing or NRG3-responsive cells, e.g. brain, heart, or kidney
CC   cells. In particular, they can be used to treat diseases which involve
CC   neural cell growth such as demyelination, or damage or loss of glial
CC   cells (e.g. multiple sclerosis). They can be used to treat patients whose
CC   nervous system has been damaged by e.g. trauma, surgery, stroke,
CC   ischaemia, infection, metabolic disease, nutritional deficiency,
CC   malignancy, or toxic agents. NRG3 can also be used to treat motor neuron
CC   disorders such as amyotrophic lateral sclerosis (Lou Gehrig's disease),
CC   Bell's palsy, conditions involving spinal muscular atrophy or paralysis,
CC   neurodegenerative disorders such as Alzheimer's disease, Parkinson's
CC   disease, epilepsy, multiple sclerosis, Huntington's chorea, Down's
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CC   syndrome, nerve deafness, and Meniere's disease. They can also be used to
CC   treat neuropathies associated with systemic disease including post-polio
CC   syndrome, hereditary neuropathies including Charcot-Marie-Tooth disease,
CC   Refsum's disease, abetalipoproteinemia, Tangier disease, Krabbe's
CC   disease, metachromatic leukodystrophy, Fabry's disease and Dejerine-
CC   Sottas syndrome, to treat disease of skeletal muscle of smooth muscle,
CC   such as muscular dystrophy or diseases caused by skeletal or smooth
CC   muscle wasting. The products can also be used for detection, diagnosis,
CC   for the production of transgenic or knockout animals or for drug
CC   screening
XX
SQ   Sequence 696 AA;

  Query Match             100.0%;  Score 277;  DB 2;  Length 696;
  Best Local Similarity   100.0%;  Pred. No. 8.9e-20;
  Matches   47;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 47
              |||||||||||||||||||||||||||||||||||||||||||||||
Db        286 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 332


RESULT 10
ABG32080
ID   ABG32080 standard; protein; 696 AA.
XX
AC   ABG32080;
XX
DT   05-NOV-2002  (first entry)
XX
DE   Novel human neuregulin related ligand NRG3B2.
XX
KW   Neuregulin related ligand; NRG3; neuroprotective; cell therapy;
KW   epidermal growth factor-like domain; EGF-like domain; Bell's palsy;
KW   ErbB4 receptor detection; amyotrophic lateral sclerosis; paralysis;
KW   lou Gehrig's disease; spinal muscular atrophy; multiple sclerosis;
KW   neurodegenerative disorder; Alzheimer's disease; Parkinson's disease;
KW   epilepsy; Huntingdon's chorea; Down's syndrome; nerve deafness;
KW   Meniere's disease; neuropathy; distal sensorimotor neuropathy;
KW   autonomic neuropathy; hereditary neuropathy; Charcot-Marie-Tooth disease;
KW   Refsum's disease; Abetalipoproteinaemia; Tangier disease;
KW   Krabbe's disease; Metachromatic leukodystrophy; Fabry's disease;
KW   Dejerine-Scottas syndrome; human; NRGB2.
XX
OS   Homo sapiens.
XX
PN   US2002082229-A1.
XX
PD   27-JUN-2002.
XX
PF   26-MAR-2001; 2001US-00817647.
XX
PR   24-JUL-1997;   97US-0053641P.
PR   30-JUN-1998;   98US-00107979.
XX
PA   (GETH ) GENENTECH INC.
XX
PI   Godowski PJ,  Mark MR,  Zhang D;
XX
DR   WPI; 2002-617760/66.
DR   N-PSDB; ABK90730.
XX
PT   A new neuregulin related ligand designated NRG3 has an epidermal growth
PT   factor-like domain and binds to ErbB4 receptor, and is useful to prevent
PT   or treat NRG3 associated disorders, particularly nerve damage.
XX
PS   Example 1; Fig 4A-B; 60pp; English.
XX
CC   The invention describes a polypeptide comprising an amino acid sequence
CC   encoding an epidermal growth factor (EGF)-like domain, and having the
CC   binding characteristics of neuregulin related ligand (NRG3). NRG3
CC   polypeptide can be used to detect ErbB4 receptor in a mammalian tissue
CC   sample, and also to prevent or treat disorders associated with NRG3 such
CC   as: amyotrophic lateral sclerosis (lou Gehrig's disease), Bell's palsy
CC   and various conditions involving spinal muscular atrophy or paralysis,
CC   neurodegenerative disorders such as Alzheimer's disease, Parkinson's
CC   disease, epilepsy, multiple sclerosis, Huntingdon's chorea, Down's
CC   syndrome, nerve deafness, Meniere's disease, neuropathy such as distal
CC   sensorimotor neuropathy or autonomic neuropathy, hereditary neuropathies
CC   such as Charcot-Marie-Tooth disease, Refsum's disease,
CC   Abetalipoproteinaemia, Tangier disease, Krabbe's disease, Metachromatic
CC   leukodystrophy, Fabry's disease and Dejerine-Scottas syndrome. This is
CC   the amino acid sequence of the novel human neuregulin related ligand
CC   NRG3B2
XX
SQ   Sequence 696 AA;

  Query Match             100.0%;  Score 277;  DB 5;  Length 696;
  Best Local Similarity   100.0%;  Pred. No. 8.9e-20;
  Matches   47;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 47
              |||||||||||||||||||||||||||||||||||||||||||||||
Db        286 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 332


RESULT 11
AAW97617
ID   AAW97617 standard; protein; 713 AA.
XX
AC   AAW97617;
XX
DT   10-MAY-1999  (first entry)
XX
DE   Mouse neuregulin related ligand NRG3.
XX
KW   Neuregulin related ligand; NRG3; mouse; ErbB4 receptor;
KW   signal transduction; nervous system disorder; neurodegeneration;
KW   neuropathy; therapy; diagnosis.
XX
OS   Mus sp.
XX
FH   Key             Location/Qualifiers
FT   Domain          1. .362
FT                   /note= "extracellular domain, specifically claimed in
FT                   Claim 5(a)"
FT   Region          66. .91
FT                   /note= "hydrophobic region"
FT   Region          105. .286
FT                   /note= "mucin-like Ser/Thr-rich region, contains sites
FT                   for O-linked glycosylation"
FT   Domain          287. .334
FT                   /note= "EGF-like domain"
FT   Domain          363. .385
FT                   /note= "transmembrane domain"
XX
PN   WO9902681-A1.
XX
PD   21-JAN-1999.
XX
PF   30-JUN-1998;   98WO-US013411.
XX
PR   09-JUL-1997;   97US-0052019P.
PR   24-JUL-1997;   97US-00899437.
XX
PA   (GETH ) GENENTECH INC.
XX
PI   Godowski PJ,  Mark MR,  Zhang D;
XX
DR   WPI; 1999-120882/10.
DR   N-PSDB; AAX06987.
XX
PT   New isolated neuregulin related ligand-3 - used to develop products for
PT   treating nervous system disorders, e.g. stroke, ischaemia, infection,
PT   malignancy, Alzheimer's disease or Down's syndrome.
XX
```

PS Claim 5(b); Page 59-62; 101pp; English.
XX
CC This is the amino acid sequence of murine neuregulin related ligand NRG3,
CC a novel member of the epidermal growth factor (EGF)-like family of
CC protein ligands that binds to the ErbB4 receptor, but not to the ErbB2 or
CC ErbB3 receptor, and which activates ErbB4 receptor tyrosine
CC phosphorylation. The sequence was deduced from the nucleotide sequences
CC of cDNA clones (see AAX06987) from a mouse brain library. The EGF-like
CC domain of NRG3 is distinct from those of NRG1 or NRG2, and NRG3 displays
CC receptor binding characteristics that are distinct from those of other
CC neuregulins. The invention provides human and murine NRG3 polypeptides
CC (see also AAW97618), expression vectors, host cells and methods for the
CC recombinant production of NRG3s. The NRG3 polypeptides and
CC polynucleotides and can be used to enhance the survival, proliferation or
CC differentiation of cells having the ErbB4 receptor in vivo and in vitro.
CC They can be used to prevent or treat damage to a nerve or damage to other
CC NRG3-expressing or NRG3-responsive cells, e.g. brain, heart, or kidney
CC cells. In particular, they can be used to treat diseases which involve
CC neural cell growth such as demyelination, or damage or loss of glial
CC cells (e.g. multiple sclerosis). They can be used to treat patients whose
CC nervous system has been damaged by e.g. trauma, surgery, stroke,
CC ischaemia, infection, metabolic disease, nutritional deficiency,
CC malignancy, or toxic agents. NRG3 can also be used to treat motor neuron
CC disorders such as amyotrophic lateral sclerosis (Lou Gehrig's disease),
CC Bell's palsy, conditions involving spinal muscular atrophy or paralysis,
CC neurodegenerative disorders such as Alzheimer's disease, Parkinson's
CC disease, epilepsy, multiple sclerosis, Huntington's chorea, Down's
CC syndrome, nerve deafness, and Meniere's disease. They can also be used to
CC treat neuropathies associated with systemic disease including post-polio
CC syndrome, hereditary neuropathies including Charcot-Marie-Tooth disease,
CC Refsum's disease, abetalipoproteinemia, Tangier disease, Krabbe's
CC disease, metachromatic leukodystrophy, Fabry's disease and Dejerine-
CC Sottas syndrome, to treat disease of skeletal muscle of smooth muscle,
CC such as muscular dystrophy or diseases caused by skeletal or smooth
CC muscle wasting. The products can also be used for detection, diagnosis,
CC for the production of transgenic or knockout animals or for drug
CC screening
XX
SQ Sequence 713 AA;

Query Match 100.0%; Score 277; DB 2; Length 713;
Best Local Similarity 100.0%; Pred. No. 9.1e-20;
Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 47
||||||||||||||||||||||||||||||||||||||||||||||||
Db 288 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 334

RESULT 12
ABG32061
ID ABG32061 standard; protein; 713 AA.
XX
AC ABG32061;
XX
DT 05-NOV-2002 (first entry)
XX
DE Mouse novel neuregulin related ligand NRG3.
XX
KW Neuregulin related ligand; NRG3; neuroprotective; cell therapy;
KW epidermal growth factor-like domain; EGF-like domain; Bell's palsy;
KW ErbB4 receptor detection; amyotrophic lateral sclerosis; paralysis;
KW lou Gehrig's disease; spinal muscular atrophy; multiple sclerosis;
KW neurodegenerative disorder; Alzheimer's disease; Parkinson's disease;
KW epilepsy; Huntingdon's chorea; Down's syndrome; nerve deafness;
KW Meniere's disease; neuropathy; distal sensorimotor neuropathy;
KW autonomic neuropathy; hereditary neuropathy; Charcot-Marie-Tooth disease;
KW Refsum's disease; Abetalipoproteinaemia; Tangier disease;
KW Krabbe's disease; Metachromatic leukodystrophy; Fabry's disease;
KW Dejerine-Scottas syndrome; mouse.
XX
OS Mus sp.
XX
FH Key Location/Qualifiers
FT Domain 1. .362
FT /label= Extracellular_domain
FT /note= "Specifically claimed in claim 5"
FT Domain 288. .334
FT /label= EGF-like_domain
FT /note= "Extracellular epidermal growth factor-like
FT domain. Specifically claimed in claim 2"
XX
PN US2002082229-A1.
XX
PD 27-JUN-2002.
XX
PF 26-MAR-2001; 2001US-00817647.
XX
PR 24-JUL-1997; 97US-0053641P.
PR 30-JUN-1998; 98US-00107979.
XX
PA (GETH) GENENTECH INC.
XX
PI Godowski PJ, Mark MR, Zhang D;
XX
DR WPI; 2002-617760/66.
DR N-PSDB; ABK90728.
XX
PT A new neuregulin related ligand designated NRG3 has an epidermal growth
PT factor-like domain and binds to ErbB4 receptor, and is useful to prevent
PT or treat NRG3 associated disorders, particularly nerve damage.
XX
PS Example 1; Fig 4A-B; 60pp; English.
XX
CC The invention describes a polypeptide comprising an amino acid sequence
CC encoding an epidermal growth factor (EGF)-like domain, and having the
CC binding characteristics of neuregulin related ligand (NRG3). NRG3
CC polypeptide can be used to detect ErbB4 receptor in a mammalian tissue
CC sample, and also to prevent or treat disorders associated with NRG3 such
CC as: amyotrophic lateral sclerosis (lou Gehrig's disease), Bell's palsy
CC and various conditions involving spinal muscular atrophy or paralysis,
CC neurodegenerative disorders such as Alzheimer's disease, Parkinson's
CC disease, epilepsy, multiple sclerosis, Huntingdon's chorea, Down's
CC syndrome, nerve deafness, Meniere's disease, neuropathy such as distal
CC sensorimotor neuropathy or autonomic neuropathy, hereditary neuropathies
CC such as Charcot-Marie-Tooth disease, Refsum's disease,
CC Abetalipoproteinaemia, Tangier disease, Krabbe's disease, Metachromatic
CC leukodystrophy, Fabry's disease and Dejerine-Scottas syndrome. This is
CC the amino acid sequence of the novel mouse neuregulin related ligand
CC (NRG3)
XX
SQ Sequence 713 AA;

Query Match 100.0%; Score 277; DB 5; Length 713;
Best Local Similarity 100.0%; Pred. No. 9.1e-20;
Matches 47; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 47
||||||||||||||||||||||||||||||||||||||||||||||||
Db 288 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 334

RESULT 13
AAW97618
ID AAW97618 standard; protein; 720 AA.
XX
AC AAW97618;
XX
DT 10-MAY-1999 (first entry)
XX
DE Human neuregulin related ligand NRG3.
XX
KW Neuregulin related ligand; NRG3; hNRG3B1; human; ErbB4 receptor;
KW signal transduction; nervous system disorder; neurodegeneration;
KW neuropathy; therapy; diagnosis.
XX

```
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Domain          1. .360
FT                   /note= "extracellular domain, specifically claimed in
FT                   Claim 5(a)"
FT   Region          66. .91
FT                   /note= "hydrophobic region"
FT   Region          101. .284
FT                   /note= "mucin-like Ser/Thr-rich region, contains sites
FT                   for O-linked glycosylation"
FT   Domain          285. .354
FT                   /note= "EGF-like domain"
FT   Domain          356. .394
FT                   /note= "transmembrane domain"
XX
PN   WO9902681-A1.
XX
PD   21-JAN-1999.
XX
PF   30-JUN-1998;   98WO-US013411.
XX
PR   09-JUL-1997;   97US-0052019P.
PR   24-JUL-1997;   97US-00899437.
XX
PA   (GETH ) GENENTECH INC.
XX
PI   Godowski PJ,  Mark MR,  Zhang D;
XX
DR   WPI; 1999-120882/10.
DR   N-PSDB; AAX06988.
XX
PT   New isolated neuregulin related ligand-3 - used to develop products for
PT   treating nervous system disorders, e.g. stroke, ischaemia, infection,
PT   malignancy, Alzheimer's disease or Down's syndrome.
XX
PS   Claim 5(b); Page 66-69; 101pp; English.
XX
CC   This is the amino acid sequence of human neuregulin related ligand NRG3,
CC   a novel member of the epidermal growth factor (EGF)-like family of
CC   protein ligands that binds to the ErbB4 receptor, but not to the ErbB2 or
CC   ErbB3 receptor, and which activates ErbB4 receptor tyrosine
CC   phosphorylation. The sequence was deduced from the nucleotide sequence of
CC   a cDNA clone (see AAX06988) from a foetal brain library. The EGF-like
CC   domain of NRG3 is distinct from those of NRG1 or NRG2, and NRG3 displays
CC   receptor binding characteristics that are distinct from those of other
CC   neuregulins. An alternatively spliced form of human NRG3 is provided in
CC   AAW97619. The invention provides human and murine NRG3 polypeptides (see
CC   also AAW97617), expression vectors, host cells and methods for the
CC   recombinant production of NRG3s. The NRG3 polypeptides and
CC   polynucleotides and can be used to enhance the survival, proliferation or
CC   differentiation of cells having the ErbB4 receptor in vivo and in vitro.
CC   They can be used to prevent or treat damage to a nerve or damage to other
CC   NRG3-expressing or NRG3-responsive cells, e.g. brain, heart, or kidney
CC   cells. In particular, they can be used to treat diseases which involve
CC   neural cell growth such as demyelination, or damage or loss of glial
CC   cells (e.g. multiple sclerosis). They can be used to treat patients whose
CC   nervous system has been damaged by e.g. trauma, surgery, stroke,
CC   ischaemia, infection, metabolic disease, nutritional deficiency,
CC   malignancy, or toxic agents. NRG3 can also be used to treat motor neuron
CC   disorders such as amyotrophic lateral sclerosis (Lou Gehrig's disease),
CC   Bell's palsy, conditions involving spinal muscular atrophy or paralysis,
CC   neurodegenerative disorders such as Alzheimer's disease, Parkinson's
CC   disease, epilepsy, multiple sclerosis, Huntington's chorea, Down's
CC   syndrome, nerve deafness, and Meniere's disease. They can also be used to
CC   treat neuropathies associated with systemic disease including post-polio
CC   syndrome, hereditary neuropathies including Charcot-Marie-Tooth disease,
CC   Refsum's disease, abetalipoproteinemia, Tangier disease, Krabbe's
CC   disease, metachromatic leukodystrophy, Fabry's disease and Dejerine-
CC   Sottas syndrome, to treat disease of skeletal muscle of smooth muscle,
CC   such as muscular dystrophy or diseases caused by skeletal or smooth
CC   muscle wasting. The products can also be used for detection, diagnosis,
CC   for the production of transgenic or knockout animals or for drug
CC   screening
XX
SQ   Sequence 720 AA;

  Query Match             100.0%;  Score 277;  DB 2;  Length 720;
  Best Local Similarity   100.0%;  Pred. No. 9.2e-20;
  Matches   47;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 47
              |||||||||||||||||||||||||||||||||||||||||||||||
Db        286 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 332


RESULT 14
AAY05452
ID   AAY05452 standard; protein; 720 AA.
XX
AC   AAY05452;
XX
DT   06-JUL-1999  (first entry)
XX
DE   Human heregulin-like factor sequence.
XX
KW   Human heregulin-like factor; HLF; cell growth regulator; diagnosis;
KW   neural system disorder; cancer.
XX
OS   Homo sapiens.
XX
PN   WO9857989-A1.
XX
PD   23-DEC-1998.
XX
PF   16-JUN-1998;   98WO-US012403.
XX
PR   17-JUN-1997;   97US-0049942P.
XX
PA   (HUMA-) HUMAN GENOME SCI INC.
PA   (GEOU ) UNIV GEORGETOWN.
XX
PI   Young P,  Ruben SM,  King CR,  Hijazi MM;
XX
DR   WPI; 1999-095327/08.
XX
PT   New isolated heregulin-like factor - used to develop products for the
PT   diagnosis and treatment of disorders involving regulation of cell growth,
PT   particularly cancers.
XX
PS   Disclosure; Page 97-99; 118pp; English.
XX
CC   This sequence is the human heregulin-like factor (HLF) of the invention.
CC   The HLF is involved in the regulation of cell growth. Detection of
CC   different levels of expression of the HLF gene can be used for the
CC   diagnosis of disorders, e.g. in the neural system. In particular,
CC   detection of different levels of HLF gene expression in cells or body
CC   fluid of an individual can be used for diagnosing cancer. The products
CC   can also be used in the treatment of disorders involving abnormal levels
CC   of HLF activity
XX
SQ   Sequence 720 AA;

  Query Match             100.0%;  Score 277;  DB 2;  Length 720;
  Best Local Similarity   100.0%;  Pred. No. 9.2e-20;
  Matches   47;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 47
              |||||||||||||||||||||||||||||||||||||||||||||||
Db        286 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 332


RESULT 15
ABG32065
ID   ABG32065 standard; protein; 720 AA.
XX
```

```
AC   ABG32065;
XX
DT   05-NOV-2002  (first entry)
XX
DE   Human novel neuregulin related ligand NRG3B1.
XX
KW   Neuregulin related ligand; NRG3; neuroprotective; cell therapy;
KW   epidermal growth factor-like domain; EGF-like domain; Bell's palsy;
KW   ErbB4 receptor detection; amyotrophic lateral sclerosis; paralysis;
KW   lou Gehrig's disease; spinal muscular atrophy; multiple sclerosis;
KW   neurodegenerative disorder; Alzheimer's disease; Parkinson's disease;
KW   epilepsy; Huntingdon's chorea; Down's syndrome; nerve deafness;
KW   Meniere's disease; neuropathy; distal sensorimotor neuropathy;
KW   autonomic neuropathy; hereditary neuropathy; Charcot-Marie-Tooth disease;
KW   Refsum's disease; Abetalipoproteinaemia; Tangier disease;
KW   Krabbe's disease; Metachromatic leukodystrophy; Fabry's disease;
KW   Dejerine-Scottas syndrome; human; gene; ss; NRG3B1.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Domain          1. .360
FT                   /label= Extracellular_domain
FT                   /note= "Specifically claimed in claim 5"
FT   Domain          286. .332
FT                   /label= EGF-like_domain
FT                   /note= "Extracellular epidermal growth factor-like
FT                   domain"
XX
PN   US2002082229-A1.
XX
PD   27-JUN-2002.
XX
PF   26-MAR-2001; 2001US-00817647.
XX
PR   24-JUL-1997;   97US-0053641P.
PR   30-JUN-1998;   98US-00107979.
XX
PA   (GETH ) GENENTECH INC.
XX
PI   Godowski PJ,  Mark MR,  Zhang D;
XX
DR   WPI; 2002-617760/66.
DR   N-PSDB; ABK90731.
XX
PT   A new neuregulin related ligand designated NRG3 has an epidermal growth
PT   factor-like domain and binds to ErbB4 receptor, and is useful to prevent
PT   or treat NRG3 associated disorders, particularly nerve damage.
XX
PS   Example 1; Fig 4A-B; 60pp; English.
XX
CC   The invention describes a polypeptide comprising an amino acid sequence
CC   encoding an epidermal growth factor (EGF)-like domain, and having the
CC   binding characteristics of neuregulin related ligand (NRG3). NRG3
CC   polypeptide can be used to detect ErbB4 receptor in a mammalian tissue
CC   sample, and also to prevent or treat disorders associated with NRG3 such
CC   as: amyotrophic lateral sclerosis (lou Gehrig's disease), Bell's palsy
CC   and various conditions involving spinal muscular atrophy or paralysis,
CC   neurodegenerative disorders such as Alzheimer's disease, Parkinson's
CC   disease, epilepsy, multiple sclerosis, Huntingdon's chorea, Down's
CC   syndrome, nerve deafness, Meniere's disease, neuropathy such as distal
CC   sensorimotor neuropathy or autonomic neuropathy, hereditary neuropathies
CC   such as Charcot-Marie-Tooth disease, Refsum's disease,
CC   Abetalipoproteinaemia, Tangier disease, Krabbe's disease, Metachromatic
CC   leukodystrophy, Fabry's disease and Dejerine-Scottas syndrome. This is
CC   the amino acid sequence of the novel human neuregulin related ligand
CC   (NRG3B1)
XX
SQ   Sequence 720 AA;

  Query Match            100.0%;  Score 277;  DB 5;  Length 720;
  Best Local Similarity  100.0%;  Pred. No. 9.2e-20;
  Matches   47;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 47
              |||||||||||||||||||||||||||||||||||||||||||||||
Db        286 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 332


RESULT 16
ADN48890
ID   ADN48890 standard; protein; 720 AA.
XX
AC   ADN48890;
XX
DT   15-JUL-2004  (first entry)
XX
DE   Human heregulin-like factor (HLF) mutant protein.
XX
KW   HLF; heregulin-like factor; diagnosis; cancer; gene therapy; human;
KW   mutant; mutein.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
PN   US6727077-B1.
XX
PD   27-APR-2004.
XX
PF   16-JUN-1998;   98US-00097681.
XX
PR   17-JUN-1997;   97US-0049492P.
XX
PA   (HUMA-) HUMAN GENOME SCI INC.
PA   (GEOU ) UNIV GEORGETOWN MEDICAL CENT.
XX
PI   Young PE,  King CR,  Hijazi M,  Ruben SM;
XX
DR   WPI; 2004-338520/31.
XX
PT   New heregulin-like factor (HLF) nucleic acid or polypeptide, useful for
PT   preparing a composition for diagnosing or treating cancer.
XX
PS   Disclosure; SEQ ID NO 22; 48pp; English.
XX
CC   The present invention relates to novel heregulin-like factor (HLF)
CC   polypeptides and the encoding polynucleotides. The invention is useful
CC   for preparing a composition for diagnosing and treating cancer. The
CC   invention is also useful in gene therapy. The present sequence is human
CC   heregulin-like factor (HLF) mutant protein.
XX
SQ   Sequence 720 AA;

  Query Match            100.0%;  Score 277;  DB 8;  Length 720;
  Best Local Similarity  100.0%;  Pred. No. 9.2e-20;
  Matches   47;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 47
              |||||||||||||||||||||||||||||||||||||||||||||||
Db        286 HFKPCRDKDLAYCLNDGECFVIETLTGSHKHCRCKEGYQGVRCDQFL 332


Search completed: May 23, 2005, 15:31:39
Job time : 71 secs
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